Allergy Abstracts

Editor

M. M. ALBERT
Brooklyn

Associate Editors

M. HARTEN
Brooklyn, N. Y.

E. H. WALZER
Bridgeport, Conn.

E. W. KAILIN
Washington, D. C.

R. A. CHAIT
Brooklyn, N. Y.

H. J. FRIEDMAN
Cleveland, Ohio

J. SHERMAN
Baltimore, Md.

B. B. SIEGEL
Far Rockaway, N. Y.

RICHARD WISEMAN
Syracuse, N. Y.

KATHERINE BOWMAN
Brooklyn, N. Y.

Advisory Editor

M. WALZER
Brooklyn, N. Y.

From the Allergy Division of
The Jewish Hospital of Brooklyn

Volume 16, Number 2 March, 1951

Asthma and Hay Fever

Effects of Pituitary Adrenocorticotropic Hormone (ACTH) on the Hypersensitive State. Howard, J. E., Harvey, A. M., Carey, R. A., and Winkenwerder, W. L.: J. A. M. A. **144**: 1347, 1950.

ACTH produced remission in 15 of 19 patients suffering from severe, intractable bronchial asthma. The duration of remission varied from 3 to 263 days, a rough correlation being noted between the amount of drug given and the duration of the remission. ACTH was administered for from 6 to 21 days in 25 mg. doses 4 times daily for the first few days with gradual reduction to 20 mg. daily. When relapses occurred, the asthma was milder than it had been before the ACTH therapy. Six patients responded as well to a second or third course of therapy as they had to the first course.

The response to cortisone of 5 patients suffering from asthma was not nearly so dramatic. Three of the patients who had failed to respond to cortisone experienced complete remission of symptoms when treated with ACTH. The fall in the blood eosinophils roughly paralleled the degree of clinical improvement. After treatment with ACTH the immediate skin reactions to foods and inhalants were significantly reduced in 5 of 6 patients tested. Ten of 15 patients tested with bacterial antigens showed significant reductions in the intensity of their reactions. The serum reagin titer of 3 patients with positive skin tests to pollens and dust was not reduced, but the direct skin test became less intense in 2 of these patients. Striking improvement was noted in the mucous membranes of the nose and nasopharynx.

Four patients treated with ACTH for severe serumlike reactions from penicillin responded dramatically, but one patient treated with cortisone

experienced only minimal relief. Ophthalmic and skin sensitivity reactions to atropine were rapidly and markedly improved by ACTH. The patch test in these patients was reduced from a marked reaction to a faint erythema after 8 days of therapy. Two cases of sympathetic ophthalmia were improved after 48 hours of treatment, but the edema and bogginess of the iris were unaffected. The fall in circulating eosinophils in sympathetic ophthalmia and atropine sensitivity roughly paralleled the clinical improvement.

H. J. F.

A Clinicopathologic Study of Bronchial Asthma With Consideration of Its Relationship to the "General Adaptation Syndrome." Winer, B. M., Beakey, J. F., and Segal, M. S.: Ann. Int. Med. 33: 134, 1950.

Forty-six cases with typical histories of bronchial asthma or tissue changes considered diagnostic of this disease were reviewed. Autopsies had been performed at the Mallory Institute of Pathology of the Boston City Hospital between 1934 and 1948. These cases were arbitrarily divided into 3 groups and the clinical records, pathology protocols, and microscopic sections were analyzed. Group I consisted of 13 patients who had died during an attack of bronchial asthma. Five of these patients were over 49 years of age and died one year or less after the onset of the asthmatic symptoms. At autopsy, all had emphysema, mucous plugs, and thickening, with hyalinization, of the basement membrane of the medium-sized bronchi. In most of the cases there were eosinophils and large groups of neutrophils both in the lumen and in the walls of the bronchi. Folding and desquamation of the epithelium and distention of the goblet cells were prominent. In several cases there were more plasma cells than lymphocytes. The bronchial musculature was not definitely thickened; the walls were sacculated with moderate congestion and edema. The walls of the respiratory bronchioles were prominent. Morphine had been administered to 3 of 5 patients in whom the diagnosis was presumed to be heart failure. There were 4 patients with right ventricular hypertrophy in the absence of hypertensive or valvular disease. Four cases had central congestion and atrophy of liver cells and one had central hemorrhagic necrosis. In the germinal centers of the mediastinal lymph nodes in 8 patients there were varying degrees of pyknosis and karyorrhexis of lymphocytes and cytophagocytosis of nuclear debris by macrophages. Similar changes were noted in one thymus and spleen which were examined. The amount of lipoid in the adrenal cortices was variable. The lymphoid changes resembled those described in the "alarm reaction" produced in animals by epinephrine, histamine, hypoxia, and emotional stress.

Group II was composed of 16 patients with diseases which frequently accompany and are possible related to chronic bronchial asthma. The clinical and pathologic pattern included elements of chronic bronchitis and emphysema, often associated with bronchopneumonia, pulmonary fibrosis, and cor pulmonale. Two patients had bronchiectasis and 2 had amyloidosis. Cor pulmonale was observed more frequently than in group I and decompensation was more often seen in the presence of coronary or valvular disease.

Seventeen patients in group III, who had a long history of bronchial asthma but died of unrelated diseases, revealed no pathognomonic findings identifiable with bronchial asthma. Most of the patients had emphysema and one-half of them had chronic bronchitis. The pathologic findings included periarteritis nodosa, rheumatic heart disease, glomerulonephritis, amyloidosis, and sarcoid tumor. In the past a hypersensitive etiology has been suggested for these entities. The authors believe that most of them should be included in the general adaptation syndrome.

I. GLAZER.

Bronchi in Course of Asthma: Experimental Bronchoscopic and Anatomic-Pathologic Study. Vallery-Radot, P., Halpern, B. N., de Montreyand, J. M. D., and Pean, V.: Presse méd. **58**: 661, 1950.

Attacks of "anaphylactic asthma" were induced in sensitized guinea pigs by exposing them to the inhalation of atomized ovalbumin. Severe "asthma" could also be induced in these animals by the administration of bronchoconstrictor drugs (histamine, choline) in aerosol form. Bronchial edema was present in the animals with "anaphylactic asthma" but not in those with "pharmacodynamic asthma." Injections of antihistaminics proved effective only during the course of "histaminic asthma" due to bronchospasm. When administered prior to the induction of "anaphylactic or histaminic asthma," these drugs prevented either reaction.

Bronchoscopy was performed on one patient with so-called allergic asthma and on one patient with so-called nonallergic asthma. In the patient with allergic asthma, narrowing of the bronchial lumen with swelling of the mucosa was observed. In the patient with nonallergic asthma, hypersecretion and bronchial spasm without any mucosal swelling were found. Microscopic examination and biopsy of material obtained from these 2 patients revealed that allergic asthma is characterized by considerable edema, while edema is completely absent in nonallergic asthma. H.

General Reactions Following Treatment of Asthma in Children With Bacterial Vaccine. Fleusborg, E. W.: Ugesk. f. læger **112**: 392, 1950.

General reactions of varying degree were noted in 42 of 162 asthmatic children treated with a stock vaccine. Reactions were usually of the delayed type, occurring 48 hours after the injection and lasting from 6 hours to 6 days. Repeated overdosage, even if it results only in slight reactions, may induce status asthmaticus or a prolonged rise of temperature. A fatal reaction attributed to an injection of vaccine was observed in a 1-year-old child. This child had shown only a slight reaction to the same dose on a previous occasion.

The author suggests that small dosages of vaccine should be used and that close attention should be paid to even slight reactions. Temperature readings taken during the first 4 days following vaccine injections often affords valuable information as to the proper dosage. H.

Respiratory Complications Associated With Demerol. McDermott, T. F., and Papper, E. M.: New York State J. Med. **50**: 1721, 1950.

Three cases which demonstrated a pronounced depression of respiration following the intravenous administration of Demerol during Pentothal and nitrous oxide anesthesia are reported. Three other cases in which intravenous Demerol precipitated asthmatic attacks during Pentothal-nitrous oxide anesthesia are also recorded. One of these patients was a known asthmatic. In another case in which asthma followed the administration of Demerol, skin tests with the drug produced markedly positive reactions. B. S.

Dermatology

Severe Urticaria Complicating Streptomycin Therapy. Lindars, D. C.: Lancet **258**: 110, 1950.

A young man developed an itchy papular rash on both forearms and legs after receiving streptomycin for 3 weeks for pulmonary tuberculosis. Benadryl given before each injection of the antibiotic suppressed the rash. However,

after 1 week, the rash reappeared and spread over the entire trunk. The face became red and edematous, there was desquamation of the skin, and edema of the external genitalia also developed. The temperature rose to 104° F. and constitutional symptoms appeared. A leucocytosis with an absolute lymphocytosis was noted at this time. Streptomycin was discontinued and Phenergan substituted for Benadryl. During the next three days, there was no improvement and penicillin therapy was started. The white count at this time was 43,750 per c.mm. with 4.5 per cent eosinophiles. Recovery took place slowly with desquamation of the involved areas of skin. Two months after the eruption cleared, an intracutaneous test was performed with a solution of streptomycin containing 50 Waksmann units per c.c. The site became red in 3 hours, the reaction reaching its height after 12 hours. The author states that a rash due to streptomycin is potentially dangerous and that great caution must be exercised if therapy is continued. B. S.

Hyaluronidase in Treatment of Human Sterility: Allergic Reaction. Criep, L. H., and Tafel, R. E.: Am. J. Obst. & Gynec. **58**: 188, 1949.

In a group of 35 women treated for sterility by packing 10 mg. of hyaluronidase into the cervix near ovulation time, a reaction occurred in 1 case several hours after each of 3 treatments. The reaction consisted of local irritation, oozing and itching of the vagina and external genitals, general malaise, abdominal cramps, coughing, sneezing, and lacrimation. The administration of Pyribenzamine was followed by a marked skin eruption. There was no known personal or family history of allergy. The patient had had pruritis ani for the past 10 years. This condition was aggravated by hyaluronidase. Intracutaneous tests performed with various dilutions of the drug were negative. A patch test applied to the skin near the external genitals was negative, but the application of hyaluronidase to the vaginal mucosa caused considerable irritation and exudation. J. S.

Skin Complications of Cortisone and ACTH Therapy. Behrman, H. T., and Goodman, J. J.: J. A. M. A. **144**: 218, 1950.

ACTH and cortisone may produce skin changes similar to those seen in hyperadrenocorticism. These include acneiform eruptions, hyperpigmentation, hirsutism, rounded or moon face, and striae atrophicae. In addition, delayed wound healing and flattening of keloidal-type scars occurred during ACTH therapy. These latter changes may be the result of some mechanism which depresses the activity of the connective tissue. Another possible explanation is that the active adrenal steroids have a pronounced inhibitory effect on the "spreading factor" of the skin. This action seems to be due to inhibition of hyaluronidase which acts on the ground substances in interstitial spaces. F.

Pathogenesis of Urticaria: Experimental Study of Life Situations, Emotions and Cutaneous Vascular Reactions. Graham, D. T., and Wolf, S.: J. A. M. A. **143**: 1396, 1950.

Thirty patients with long-standing histories of repeated attacks of urticaria were psychometrically evaluated and found to be harboring feelings of intense resentment which could be closely correlated causally with their attacks. During these attacks, dilatation of both the arterioles and the

minute vessels of the skin as demonstrated by means of skin temperatures and the reactive hyperemic threshold of the skin appeared to be the actual cause of the whealing. Other emotional reactions, such as anxiety, hostility, grief, or dejection were never found to be directly associated with the urticaria. The feeling of resentment which these patients harbored was not associated with the desire to resort to retaliatory or remedial action. They failed to express or feel any hostility and were preoccupied with what was being done to them rather than with what they could do about the situation. Allergic factors could not be established as causative in any of these patients, most of whom had been referred to the investigators because there was some evidence that emotional factors were of importance. There were no known drug-sensitive patients in the series. Iontophoretic skin tests with histamine and pilocarpine were performed on 24 of the patients. Twenty-three responded with some whealing to 0.001 per cent histamine and to 1.0 per cent pilocarpine. Only 6 of 25 control subjects responded to the 0.001 per cent histamine and only 3 to the 1.0 per cent pilocarpine. F.

Otorhinology and Ophthalmology

The Prophylaxis and Treatment of Acute Respiratory Diseases With Antihistaminic Drugs. I. Prophylactic Treatment in Naval Male Recruits. The Personnel of United States Naval Medical Research Unit No. 4, J. Lab. & Clin. Med. **36**: 555, 1950.

A study was conducted to determine the prophylactic efficacy of antihistaminic drugs in respiratory infections. A group of 352 male naval recruits received thonzylamine hydrochloride in 50 mg. doses twice a day. One control group of equivalent size received a placebo and a third group received no therapy. The study was conducted for a 10 week period from February to April, 1950, during which time there was a high incidence of respiratory diseases, most of them classified as the common cold. An epidemic of influenza due to influenza virus type A complicated the study and it was not possible to effect a completely satisfactory clinical separation of influenza and other types of respiratory disease. No significant difference in the incidence of infection could be determined in successive surveys between the treated and untreated groups. No evidence was found that the antihistaminics prevent these diseases or effect any important alteration in their symptomatology. E. W.

The Prophylaxis and Treatment of Acute Respiratory Diseases With Antihistaminic Drugs. II. Prophylactic Treatment With Therapeutic Dosage in Navy Male Recruits. The Personnel of United States Naval Medical Research Unit No. 4, J. Lab. & Clin. Med. **36**: 570, 1950.

Thonzylamine hydrochloride and Trimeton in therapeutic dosage were compared with a placebo for prophylactic efficacy against the common cold. The subjects were 3 groups of naval recruits who received a drug 3 times a day for one week from April 10 to April 18, 1950. No significant differences were found among the 3 groups in the incidence of colds, in the type of symptomatology, or in the recovery rate. It was concluded that the use of therapeutic doses of antihistaminics does not result in the "abating" of colds or in any important alteration in their symptomatology and duration. E. W.

The Prophylaxis and Treatment of Acute Respiratory Diseases With Antihistaminic Drugs. III. Treatment of Acute Respiratory Infection in Navy Wave Recruits. The Personnel of United States Naval Medical Research Unit No. 4, J. Lab. & Clin. Med. **36**: 576, 1950.

Navy Wave recruits who presented symptoms of the common cold received thonzylamine hydrochloride, atropine sulfate, or placebo tablets. In all, 165 patients participated in the study. Treatment was started from 1 to 84 hours after the onset of symptomatology. The majority of patients began treatment within the first 24 hours. Careful nasal examinations and eosinophil counts were made. No significant statistical difference in the duration of symptomatology or in the course of the disease was found among the 3 groups of patients. None of the agents tested abated colds. No correlation existed between eosinophil counts in nasal smears and allergy or to response to therapy. Antihistaminic drugs had an atropine-like effect on the nasal mucosa.
E. W.

The Prophylaxis and Treatment of Acute Respiratory Diseases With Antihistaminic Drugs. IV. The Prophylaxis and Treatment of Colds in Volunteers. The Personnel of United States Naval Medical Research Unit No. 4, J. Lab. & Clin. Med. **36**: 584, 1950.

A group of antihistaminic drugs was compared with placebos as to their efficacy in the prevention or cure of the common cold in naval volunteers who had extensive contact with the civilian population. No physical examinations were performed. All information was collected by questionnaires. One hundred and sixty-five people took part in the prophylactic study and 370 in the therapeutic study. Critical analysis of results in the prophylactic series was not possible because too few of the subjects had taken the preparations for an adequate period of time. Among those who took part in the therapeutic series, equally beneficial results were reported from placebos and antihistaminic drugs. This improvement was attributed to psychologic factors.
E. W.

The Early Treatment of Common Colds With an Antihistamine—Histadyl. Browning, R. H.: New England J. Med. **243**: 994, 1950.

Over 600 freshman students were divided into 3 groups and studied for colds during one year. Subjects in the first group were given 50 mg. Histadyl every 4 hours as long as the cold symptoms persisted. Those in the second group were treated similarly with a placebo, while the third group was untreated. The students in the group which received placebos had the lowest rate of hospital care and the fewest number of days of care per student hospitalized. The average number of colds per student and the percentage of those who had colds were similar in all 3 groups. The students' appraisals of the treatment (comparison with previous colds, incipient colds reported as aborted or "prevented") were similar in the first 2 groups. I. GLAZER.

Miscellaneous Allergies

The Problem of Allergy With a Report on Skin Testing With Salicylate-Containing Human Sera. Mathews, K. P., Lovell, R. G., and Sheldon, J. M.: J. Lab. & Clin. Med. **36**: 416, 1950.

Twelve patients with a history of aspirin sensitivity were tested by the prick and intracutaneous techniques with sera containing aspirin in levels

ranging from 6 to 24 mg. per cent. These sera had been obtained from individuals who had received aspirin in large doses for a period of at least 3 weeks prior to bleeding. Readings of the reactions to these tests were made immediately and also 24 and 48 hours later. In no instance did the reactions obtained with aspirin-containing sera exceed those obtained with normal sera. In "reversed" passive transfer studies, rheumatic patients who were receiving large doses of aspirin by mouth were tested with the sera of aspirin-sensitive patients by the prick and intracutaneous methods. No differences were noted in the degree of whealing with test or control sera. In passive transfer studies where previously prepared sites were tested with aspirin-containing sera, control sera, and saline solutions of aspirin (1:300) negative results were obtained. It was concluded that the clinical history is the only satisfactory method of diagnosing aspirin sensitivity at the present time. E. W.

Therapeutic Effect of Pituitary Adrenocorticotropic Hormone (ACTH) in a Case of Henoch-Schonlein Vascular (Anaphylactoid) Purpura. Stefanini, M., Roy, C. A., Zannos, L., and Dameshek, W.: J. A. M. A. **144**: 1372, 1950.

ACTH was administered in a case of Henoch-Schönlein vascular (anaphylactoid) purpura. The patient, a 3-year-old boy, suddenly developed recurring purpuric skin lesions, painful swelling of the ankles, and crampy abdominal pains. There was evidence of melena, hematuria, glomerulonephritis, and increased capillary fragility (tourniquet test). Other laboratory findings were essentially normal. Treatment with sulfadiazine, penicillin, and aureomycin did not influence the condition. Shortly after the institution of ACTH therapy in doses of 5 mg. 3 times daily the abdominal pains disappeared and there was a rapid fading of the skin lesions. Skin biopsies were taken before and after therapy. The latter showed a marked decrease in the inflammatory reaction about the capillaries. In spite of the decided improvement, the disease was not regarded as having been cured, since the chronic glomerulonephritis so often seen as a sequela of this condition was still evident. F.

Influence of Streptomycin on Skin Reactivity to Tuberculin. Experimental and Clinical Studies. Vacarezza, R. F., Cettrangolo, A., and Stupenengo, M. H.: Prensa méd. argent. **37**: 1299, 1950.

The cutaneous reactivity to tuberculin was studied in guinea pigs inoculated with virulent tubercle bacilli and treated with streptomycin. Comparison of the skin reactivity in these animals with that present in control animals revealed a diminution of reactivity in the streptomycin-treated animals. The earlier streptomycin was administered, the later tuberculin sensitivity appeared. Skin reactivity to tuberculin returned to normal after streptomycin was discontinued.

In 54 patients with pulmonary tuberculosis, tuberculin sensitivity was investigated before, during, and after streptomycin therapy. During treatment, the skin reactivity to tuberculin diminished in all but 2 of the patients studied. The 2 exceptions were patients with miliary tuberculosis, in whom the skin reactivity to tuberculin increased. The reactivity returned to normal when streptomycin was discontinued. When a mixture of tuberculin and streptomycin was used for skin testing a greatly diminished tuberculin reaction was obtained. Streptomycin is believed to neutralize the antigenic activity of tuberculin in the blood and in vitro. H.

Periarteritis Occurring During Propylthiouracil Therapy. McCormick, R. V.: J. A. M. A. **144**: 1453, 1950.

Propylthiouracil, administered 4 times daily to an elderly female, produced diarrhea and fever (103.4° F.) within 24 hours. After approximately 12 doses, the patient became incontinent, irrational, had difficulty articulating, showed a left facial paresis, and had a Babinski reflex on the left side. Spinal fluid examination, the Wassermann reaction, and the white blood count and differential were all within normal limits. After the fifth day, it was suspected that the propylthiouracil might be causally related. Withdrawal of the drug was followed, within 24 hours, by complete disappearance of symptoms. One week later, a test dose of 50 mg. of the drug was given; within 12 hours, mild symptoms again were manifest. About 2 months later, the patient was inadvertently given propylthiouracil 4 times a day for 6 days. She developed signs and symptoms of a left cerebral accident for which she was hospitalized. A spinal tap showed no abnormalities. After 6 days, the patient died without regaining consciousness. Post-mortem examination revealed a diffuse periarteritis. H. J. F.

Beet Sensitivity: Allergic Reactions From the Ingestion of Beet (Sucrose) and Monosodium Glutamate of Beet Origin. Randolph, T. G., and Rollins, J. P.: J. Lab. & Clin. Med. **36**: 407, 1950.

Four atopic patients with allergic symptomatology were found to be clinically sensitive to beets and beet products. Symptoms were produced by the test feeding of either beet sugar or monosodium glutamate of beet origin. The latter product, a condiment, is used in the preparation of meat flavors in soups, chowders, bouillons, sauces, creamed foods, and cheese dishes. The failure of manufacturers to indicate the source of the materials employed in the manufacture of sodium glutamate, alcoholic spirits, and sugar makes the avoidance of beet products extremely difficult for beet-sensitive patients. E. W.

Anaphylaxis

Effect of 17-Hydroxy-11-Dehydrocorticosterone (Compound E) and of ACTH on Arthus Reaction and Antibody Formation in the Rabbit. Germuth, F. G., and Ottinger, B.: Proc. Soc. Exper. Biol. & Med. **74**: 815, 1950.

Twenty-four rabbits were sensitized to egg albumin with daily intracutaneous injections administered for 18 days. Eight of these animals were simultaneously treated with compound E, 8 with ACTH, and 8 were used as controls. By the thirteenth injection, all 8 control animals had developed large Arthus reactions. Hemorrhage and necrosis were present in 6 of these rabbits. The 8 compound E-treated animals showed only slight or negative skin reactions to egg albumin. Arthus reactions with hemorrhage and necrosis developed in 3 of the ACTH-treated rabbits. High titers of antibody nitrogen were found in 5 control animals. About 50 per cent less antibody was found in the ACTH-treated rabbits. The sera from the compound E-treated animals contained only minimal amounts of antibody. As a confirmation of the precipitin reaction, the ability of the sera of the 3 groups of rabbits to produce passive anaphylaxis in guinea pigs was investigated. All of the sera taken from control and ACTH-treated animals induced passive anaphylaxis in guinea pigs. All sera from compound E-treated animals failed to sensitize guinea pigs. Passive Arthus reactions were produced in both control and treated rabbits with antipneumococcus serum. Apparently, the skin reactivity of the animals was not altered by the hormone therapy. It was concluded that

the inhibitory effect of compound E and of ACTH on experimental hypersensitivity of the Arthus type results from the capacity of these hormones to suppress antibody formation. B. S.

Formation of Bradykinin in Anaphylactic and Peptone Shock. Beraldo, W. T.: Am. J. Physiol. **163**: 283, 1950.

A hypotensive and smooth muscle-stimulating substance, which possesses pharmacologic properties similar to bradykinin with which it is probably identical, was demonstrated in the plasma of dogs following anaphylactic and peptone shock. This substance shows the following characteristics: (1) it produces a slow contraction of the guinea pig, rat, and rabbit intestinal or uterine strips, which is not antagonized by antihistaminics or atropine; (2) it causes a fall in blood pressure in cats, rabbits, and dogs; (3) it is dialyzable, thermostable in neutral or slightly acid solution, insoluble in ether and acetone, and is destroyed by incubation with venom or trypsin; and (4) its effect on the guinea pig intestine is not diminished upon repeated exposures in the perfusion bath.

This substance was also demonstrated in vitro when peptone was added to plasma globulin. The bradykinin activity of the blood bore no relationship to the severity of the preceding anaphylactic or peptone shock. There was, however, a direct relationship between the amount of peptone injected and the amount of active substance produced. This supports the hypothesis that peptone acts directly on the blood globulin. The in vitro production of the substance appears to be dependent upon an optimal incubation period and an optimal concentration of peptone. Fibrinolysin, when added to the perfusion bath, produced little or no contraction of the strip, but when this material was first mixed with globulin and incubated for 1 to 2 minutes, contractions could be elicited. If the incubation was prolonged for 2 to 3 hours, there was a loss of active principle indicating that it had been destroyed by fibrinolysin. Crystalline soybean trypsin inhibitor, when added to globulin, inhibited the appearance of the gut-stimulating substance after addition of peptone.

These findings indicate that, in addition to histamine, a hypotensive, smooth muscle-stimulating substance probably identical with bradykinin is formed during the course of anaphylactic and peptone shock in dogs. This substance very likely plays a role secondary to histamine in the pathogenesis of shock. H. J. F.

Vitamin B_{12} and Antihistamine Activity. Sharpe, H. M., Woollett, E. A., and Cuthbertson, W. F. J.: Nature **166**: 651, 1950.

The intraperitoneal injection of vitamin B_{12} 15 minutes prior to the intracardiac administration of histamine failed to prevent histamine shock in guinea pigs. Vitamin B_{12} given intravenously to cats under chloralose anesthesia failed to abolish the fall in the arterial blood pressure produced by the intravenous injection of histamine. I. GLAZER.

Pharmacology, Physiology, and Pathology

The Shwartzman Phenomenon. I. Inhibitory Action of Nitrogen Mustard (HN_2). Schlang, H. A.: Proc. Soc. Exper. Biol. & Med. **74**: 749, 1950.

The Shwartzman phenomenon was inhibited in all rabbits treated with HN_2 4 days before the intravenous injection of bacterial filtrate. When the access of HN_2 to the skin site where the preparatory injection had been given

was prevented by the use of a special clamp, the Shwartzman reaction was still inhibited. When the abdominal aorta was occluded, thus protecting the lower limbs from the action of HN_2 but allowing the agent free access to the site of the preparatory injection, the Shwartzman phenomenon was produced. It is postulated that the inhibitory effect of HN_2 on the Shwartzman phenomenon is the result of a systemic rather than a local action of the agent.
B. S.

Thrombocytopenic Purpura Due to Allergy to Quinidine: Study of the Mechanism of Thrombocytopenia. Hirsch, E. O., and Dameshek, W.: Am. J. Med. **9**: 828, 1950.

Quinidine was found to be the cause of a case of idiopathic thrombocytopenic purpura. The patient, a 58-year-old woman, had taken quinidine regularly for about 1 month without untoward effects. Readministration of the drug 3 months later was followed by the appearance of generalized purpura and bleeding gums. These signs rapidly disappeared when the patient discontinued the use of the drug. One month later, the administration of quinidine again produced a severe, generalized pruritus which was accompanied by a weeping, hemorrhagic, eczematous rash about the mouth. Quinidine was not suspected at this time. Examination revealed a marked reduction in the platelet count, increased bleeding time, a positive tourniquet test, delayed clot retraction, and a lowered serum-prothrombin time. Bone marrow smears were normal except that the megakaryocytes, which were present in normal numbers, were perfectly round and smooth, the cytoplasmic outline being minus the usual scalloping and lacunae. The megakaryocytes appeared to be devoid of platelet production. There was no increase in the eosinophils in either the peripheral blood or in the bone marrow. Because of the history, quinidine was suspected as the cause and withdrawal of the drug resulted in a rapid regression of symptoms. When recovery was complete, readministration of the drug promptly produced a recurrence of symptoms. It is believed that sensitivity to the drug resulted in an inhibition of platelet production from the megakaryocytes and a rapid destruction of platelets already present in the blood.
H. J. F.

The Lymphocytic Origin of a Plasma Factor Responsible for Hypersensitivity in Vitro of Tuberculin Type. Miller, J. M., and Favour, C. B.: J. Exper. Med. **93**: 1, 1951.

Blood was obtained from guinea pigs sensitized with heat-killed tubercle bacilli and from human beings who had active tuberculosis and whose leucocytes underwent lysis on exposure to tuberculin. Leucocytes from these bloods were washed with saline solution and suspended in normal plasma. When these cells were incubated with tuberculin no lysis occurred for several hours. This is in contrast to the lysis exhibited, within from 20 minutes to 1 hour after incubation with tuberculin, by sensitive cells suspended in plasma from a sensitive host. The washed, sensitive cells released, within a 7 hour period, into their normal plasma diluent a substance which when added to normal leucocytes rendered them susceptible to lysis by tuberculin. This substance is referred to as "shed plasma factor" and is not obtainable from normal leucocytes. This factor precipitates with the euglobulin plasma fraction. Neutrophils and lymphocytes were carefully separated from tuberculin-sensitive human blood. Plasma shed factor was found to be released only from lymphocytes. It is suggested that this observation may relate to antibody production by lymphocytes. Preliminary experiments indicate that there is no cytologic phenomena in antibovine albumin-albumin systems.
E. K.

Influence of Histamine and Acetylcholine on Nerve Block Due to Procaine. Nortqvist, P.: Nature **166**: 990, 1950.

The central part of a frog ischiadicus nerve was placed in a phosphate Ringer's solution containing 0.05 per cent procaine dihydrochloride. The nerve was stimulated with a break shock every second and every spike was photographed. When total block occurred (9.6 minutes), the solution was replaced with phosphate Ringer solution containing 0.5 per cent histamine dihydrochloride in addition. Recovery began almost immediately and was maximal in 1.9 minutes. Acetylcholine had a similar but slower effect on the procaine block. I. GLAZER.

Polyarteritis Nodosa Involving the Female Genital Tract. Fisher, E. R., and Laufe, L. E.: Am. J. Obst. & Gynec. **60**: 445, 1950.

A 61-year-old woman was hospitalized while in a coma and died within a few minutes. The only known medication which she had taken was 30 gr. sodium salicylate daily for the previous 3 days. Autopsy revealed acute polyarteritis nodosa involving the kidneys, spleen, intestinal tract, uterus, cervix, and ovaries. Diffuse involvement of the female genital tract has not been previously reported. The diagnosis of polyarteritis nodosa should be entertained in women having gynecologic complaints associated with bizarre systemic symptoms. J. S.

Effectiveness of Antihistaminic Compounds Introduced Into Normal Human Skin by Iontophoresis. Shelley, W. B., McConahy, J. C., and Hesbacher, E. N.: J. Invest. Dermat. **15**: 343, 1950.

Nine antihistaminic drugs were introduced into the skin by iontophoresis. Five minutes later they were assayed iontophoretically with histamine. The antihistaminic activity demonstrated by these drugs in the order of decreasing potency was as follows: Pyribenzamine, Diatrin, Neoantergan, Thenylene, Decapryn, Benadryl, Tagathen, Neohetramine, Thephorin. It is suggested, therefore, that Pyribenzamine, Diatrin, or Neoantergan should be the most effective of these compounds for topical use. R. WISEMAN.

Tuberculin Sensitivity in Boeck's Sarcoid. Bjornstad, R. T.: Acta. tuberc. Scandinav. **24**: 15, 1950.

Seventy-one patients with Boeck's sarcoid associated with definite skin lesions were tested by the intracutaneous technique with tuberculin up to 10 mg. Fifty (70.4 per cent) showed negative reactions and 21 (29.6 per cent) showed positive reactions. The positive reactors included 12 with positive reactions to 0.1 mg. tuberculin and 2 with positive reactions to 0.01 mg. Nine of the 50 patients with negative reactions had been exposed to tuberculosis in their homes. The frequency of the negative reactions to tuberculin is considered to be due to the presence of sarcoid and not due to the fact that these patients have escaped tuberculous infection. The tuberculin anergy and resistance to tuberculosis in Boeck's sarcoid may or may not have a purely tuberculous etiology. H.

Absorption, Distribution and Excretion of Phenindamine (Thephorin). Dailey, R. E., Way, E. L., Parikh, J. R., Sung, C., and Howie, D. L.: Proc. Soc. Exper. Biol. & Med. **74**: 394, 1950.

Rats, fasted for 18 to 24 hours, were given phenindamine by stomach tube. The animals were sacrificed at various time intervals and their gastrointestinal

contents were examined for the presence of phenindamine by a modification of the Brodie methyl orange technique. Approximately 75 per cent of the drug disappeared from the gastrointestinal tract within 4 hours and about 10 per cent was still present in the tract after 24 hours. After administration of the drug intraperitoneally, the animals were sacrificed at definite time intervals and the blood and tissue of various organs were analyzed. Phenindamine was found to leave the blood rapidly and to localize in high concentration in the lungs, liver, kidneys, spleen, and brain. It could not be detected in the tissues 24 hours after administration. In human beings and rats only minimal amounts of phenindamine were recovered in the urine and less than 10 per cent was recovered in the feces. The authors conclude that this antihistaminic drug is almost completely metabolized in the body. B. S.

Experiments With Nor-Epinephrine. Kroneberg, G., and Roenicke, G.: Klin. Wchnschr. **28**: 353, 1950.

The injection of Arterenol (nor-epinephrine) in normal subjects resulted in increased systolic and diastolic blood pressures. The subcutaneous and intravenous injection of epinephrine produced an increased systolic pressure and a decreased diastolic pressure. The administration of epinephrine was followed by tachycardia, while Arterenol caused bradycardia. The hyperglycemic action of Arterenol and its effect on the basal metabolic rate was much less pronounced than that of epinephrine. The increased blood pressure following epinephrine appears to be due to an increase in the minute volume and pulse rate. The increased blood pressure caused by Arterenol can be explained by increased peripheral resistance. H.

The Clinical Response of Human Beings to L-Nor-Epinephrine and its Clinical Possibilities. Kappert, A., Sutton, G. C., and Reale, A.: Acta cardiol. **5**: 121, 1950.

The effects of nor-epinephrine (Arterenol) on blood pressure, heart rate, electrocardiogram, hematocrit values, blood volume, oxygen consumption, and sugar metabolism were compared with those of epinephrine in healthy human subjects ranging from 18 to 32 years of age. Nor-epinephrine is especially indicated in diabetics because of its slight effect on sugar metabolism. The drug should be of value in the treatment of various types of shock. H.

Studies of Mode of Action of Cortisone (Compound E) and Pituitary Adrenocorticotropic Hormone (ACTH). Heilmeyer, L., Frey, J., and Weissbecker, L.: Deutsche med. Wchnschr. **75**: 1124, 1950.

A patient with pulmonary and intestinal tuberculosis was treated with cortisone. Treatment resulted in a decrease of eosinophils, a drop in the sedimentation rate, and a reduction in the high excretion rate of ketosteroids. An artificially induced inflammatory reaction in the skin of this patient was also greatly reduced by the action of cortisone. This indicates that the antirheumatic effect of cortisone is nonspecific and suggests that cortisone influences a regulatory process that controls various functions. From studies performed on another patient with arthritis, the writers conclude that the action of cortisone on rheumatic disorders is not etiotropic. H.

The Role of Antibodies in Insulin Resistance. Berne, R. M., and Wallerstein, R. S.: J. Mt. Sinai Hosp. **17**: 102, 1950.

A patient who showed evidence of insulin resistance and required from 400 to 900 units daily of insulin was studied. Localized allergic reactions

at the injection sites manifested by urticaria and induration occurred at various times and were relieved by Pyribenzamine. Changing brands of insulin in order to vary the animal source was without noticeable effect. Passive transfer and precipitin tests made with the patient's serum gave negative results. Attempts to demonstrate insulin neutralizing antibodies in rabbits also were unsuccessful. It is suggested that the presence of insulin neutralizing or allergic antibodies are apparently not the mechanism in the causation of insulin resistance. R. WISEMAN.

Periarteritis Nodosa Associated With Ratbite Fever Due to Streptobacillus Moniliformis (Erythema Arthriticum Epidemicum). Prouty, M., and Schafer, E. L.: J. Pediat. **36**: 605, 1950.

The coexistence of rat-bite fever and periarteritis nodosa is reported in a 9-year-old child. The presence of rat-bite fever was proved by agglutination tests and the periarteritis nodosa was verified at autopsy. The child was bitten by a white rat one week prior to the onset of symptoms and was given penicillin intermittently during the course of the illness. There was no history of the administration of sulfonamides, sera, antitoxins, or other drugs either during or prior to the illness. There was no personal or family history of allergy. Whether the rat-bite fever was concurrent with, or antedated, or perhaps initiated the periarteritis nodosa could not be determined. The course of the illness seemed to indicate that rat-bite fever was the initial disease and that periarteritis nodosa subsequently developed. The possible etiology of periarteritis nodosa is discussed and the literature is reviewed. J. S.

Sites of Antibody Production. Oakley, C. L., Warrack, G. H., and Batty, I.: J. Path. & Bact. **61**: 179, 1949.

Following a second injection of diphtheria toxoid into laboratory animals in one hind leg, the total amount of diphtheria antitoxin recovered from the lymph glands draining the injected limb was greater than that obtained from the corresponding glands draining the uninjected limb. When diphtheria toxoid was then injected into the right hind leg and tetanus toxoid in the left hind leg of horses, the tetanus/diphtheria antitoxin ratio in the lymph glands draining the leg injected with tetanus toxoid was higher than the ratio of these antitoxins in the serum. In the lymph glands draining the leg injected with diphtheria toxoid, the ratio was lower than that in the serum. It was concluded that the lymph glands draining the infected area probably produce or store antitoxin. There was evidence that antitoxin might also be produced in the skin at the site of the injection. Antibody production elsewhere in the body could not be demonstrated. Production of antitoxin may continue for as long as 8 months after the injection of antigen. J. S.

Miscellaneous

The Effect of Cortisone and Adrenocorticotropic Hormone on the Concentration of Circulating Antibody. Bjrneboe, M., Fischel, E. E., and Stoerk, H. C.: J. Exper. Med. **93**: 37, 1951.

Polyvalent pneumococcal vaccine was injected repeatedly in rabbits treated with adrenocorticotropic hormone (ACTH) or with cortisone. Antibody was measured as specific antibody nitrogen. Five of 48 control animals died in the first 2 weeks as a result of the toxicity of the injections. Ten of 34 hormone-treated animals succumbed during the same period. After the

first 2 weeks, the administration of cortisone did not affect the mortality rate. Individual titers both in treated and control groups varied greatly, but repeated comparisons of treated and control groups led to the conclusion that ACTH and cortisone diminish antibody titers. When cortisone was administered 2 weeks after the onset of immunization antibody, titers in 6 of 10 test animals fell, sometimes within 2 or 3 days. In another comparison, antibody titers fell within several hours of the administration of ACTH. Inasmuch as the half life of antibody protein is about 2 weeks, it is suggested that actual destruction of antibody protein may be taking place, instead of or in addition to inhibition of antibody synthesis. Pathologic examination revealed that the hormone-treated animals had atrophic malpighian bodies with fragmentation of lymphocytes in the splenic follicles, absence of hyperplasia of germinal centers in the follicles and, in general, reversal or inhibition of most of the alterations observed in the hyperimmunized control animals. E. K.

An Experimental Study of Antibiotics for Their Activity in the Shwartzman Phenomenon. Kerby, G. P., and Muller, J. C.: J. Invest. Dermat. **15**: 385, 1950.

Meningococcal filtrate of known high Shwartzman potency was used for testing the Shwartzman activity of intravenous aureomycin, dihydrostreptomycin, penicillin crystalline G, Chloromycetin kapseals, crystalline Chloromycetin and terramycin. In one experiment, a group of rabbits received a provocative intravenous injection of meningococcal filtrate approximately 24 hours after having received preparatory intracutaneous injections of meningococcal filtrate and of various antibiotics. There was no evidence of reaction at any of the sites prepared with antibiotics, but a definite Shwartzman phenomenon occurred at the filtrate-injected areas. In the second experiment, rabbits received a provocative injection of each of the antibiotics. Twenty-four hours previously, each rabbit had been given an intracutaneous inoculation of the corresponding antibiotic and of the meningococcal filtrate. No Shwartzman reaction was provoked at any of the sites. Each of these rabbits was subsequently tested in the usual manner with the same meningococcal filtrate. Each showed a positive response. It was concluded that present-day antibiotics contain no Shwartzman-active principle. R. WISEMAN.

Direct Evidence for the Antigenicity of the Glomeruli in the Production of Nephrotoxic Serums. Greenspon, S. A., and Krakower, C. A.: Arch. Path. **49**: 291, 1950.

A method for separating renal glomeruli from other renal components is described. Employing a suspension of dog glomeruli as an antigen, a potent antiserum was produced in rabbits. This serum was capable of producing lesions of nephritis in dogs. Such a serum could not be obtained when other components of renal cortex, free of glomeruli, were employed as the antigens. It seems evident that, in the production of a nephrotoxic antiserum, the antigenicity of the renal cortex lies within the glomerulus. J. S.

I^{131} as an Antigen Label in the Circulating Serum of Non-Immune Rabbits. Knox, W. C., and Endicott, F. C.: J. Immunol. **65**: 523, 1950.

Two groups of rabbits were given intravenous injections of bovine serum albumin (B.S.A.). One group received radioiodinated serum and the other group was given untreated serum. Samples of sera were collected at various times following the injections and antigen N determinations were made by

means of quantitative precipitin reactions and by calculating the concentration of I^{131}. The results showed that the concentration of antigen N was essentially the same in each series, regardless of the method of determination employed. In summation, the authors state that the measurement of I^{131} in the serum of non-immune rabbits following intravenously administered B.S.A. I^{131} is an adequate index of antigen N and that there is very little difference, if any, between the clearance of B.S.A. and B.S.A. I^{131}. R. WISEMAN.

Generalized Histoplasmosis in Infants and Children. Review of Ten Cases, One With Apparent Recovery. Klingberg, W. G.: J. Pediat. **36**: 728, 1950.

Ten proved cases of histoplasmosis are reviewed. One patient recovered and 9 died. All fatal cases showed negative skin tests to histoplasmin as well as to other fungus antigens, such as coccidiodin and blastomycin. The patient who survived showed similar negative reactions, but developed a positive skin test to histoplasmin after subsidence of the acute illness. The tuberculin test was negative in all cases.

The findings are analogous to those observed in tuberculosis. It takes several weeks or months after an initial infection before sufficient antibodies are produced to give a positive reaction, and a positive skin reaction indicates either present or past disease. The negative reactions obtained in the fatal cases apparently indicate that either the infection is so overwhelming that no antibodies are produced or that death occurred before sufficient time elapsed for the production of antibodies. J. S.

The Formation of Circulating Antibody in the Splenectomized Human Being Following Intravenous Injection of Heterologous Erythrocytes. Rowley, D. A.: J. Immunol. **65**: 515, 1950.

Fourteen splenectomized human subjects and a control group were injected intravenously with 1 c.c. of a 2 per cent suspension of washed sheep erythrocytes. Splenectomy had been performed from 8 to 40 months prior to sensitization. Ophthalmic, scratch, and intracutaneous tests were made with sheep antigen before it was injected to establish the absence of hypersensitivity. Antibody titers were done before sensitization and were repeated at various intervals following the injection. The results showed that the splenectomized subjects had low hemagglutinin and hemolysin titers as compared to the titers found in normal individuals. No evidence of the presence of a blocking antibody was demonstrated in any of the sera of the control or of the splenectomized patients. The possible significance of these findings in the etiology of acquired hemolytic anemia, idiopathic thrombocytopenia, and erythroblastosis fetalis is discussed. R. WISEMAN.

Psychologic Factors of Migraine in Children. Katz, J., Friedman, A. P., and Gisolfi, A.: New York State J. Med. **50**: 2269, 1950.

Fifteen children with classical symptoms of migraine were studied. Eleven were females and 4 were males. The ages of these patients ranged from 5½ to 15 years. The family history of 11 patients revealed that at least one relative had severe headaches; among the relatives of 6 of these families, a diagnosis of migraine was made. Medical studies performed on these patients revealed nothing of significance. In 9 children, gross evidence of neurosis could be detected during a brief interview. There was evidence of an adequate adjustment in only 3 patients. Special psychologic tests or psy-

chiatric techniques were not used to gain this information. The neurotic symptoms included temper tantrums, numerous phobias, nightmares, hair-pulling, enuresis, obvious anxiety, hyperactivity, lethargy, thumb-sucking, nail-biting, and feeding difficulties. A definite chronologic relationship between emotional upsets and the occurrence of headaches was not found, but it is felt that a relationship does exist and probably requires more detailed study to bring this factor to light. B. S.

Diatrin, a New Antihistaminic With Minimal Side Reactions. Marton, S.: Ann. Int. Med. **33**: 1444, 1950.

Patients with allergic manifestations received 50 mg. of Diatrin, Pyribenzamine, or Benadryl orally 3 times daily. Of the 113 patients treated with Diatrin, 13 had some side effects. Ten of 11 patients with urticaria treated with Diatrin showed improvement, 55 of 72 hay fever patients reported relief, and 1 patient with food allergy reported complete relief. The results in allergic rhinitis were fair. In other allergic conditions, the results were rather poor. I. GLAZER.

Bronchiectasis in Children. Charas, A.: Arch. argent. de pediat. **21**: 161, 1950.

A group of 40 children suffering from bronchiectasis was studied. The disease was of the congenital type in 6 and of the acquired type in 34. The most frequent etiologic factors were chronic or recurring respiratory infections, atelectasis, pertussis, and measles. The lower lobe of the right or left lung was most often involved. Bronchiectasis appears to develop in 2 stages, that is, reversible and irreversible bronchopulmonary disease. During the earliest phase of reversibility, which is of short duration, it is amenable to medical treatment. Surgical treatment is indicated in the later stages of reversibility. Pneumonectomy, or a unilateral or bilateral lobectomy, was performed on 30 children. These procedures are well tolerated by children. H.